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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,758	02/19/2003	James M. Roberts	14538A-004510US	8779

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EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 12/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,758	ROBERTS ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *September 14, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *1-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0803,0903*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III, claims 15 and 16, in the reply filed on September 14, 2005 is acknowledged. No grounds for traversal are stated. Claims 1-14 are withdrawn from consideration as being directed to nonelected inventions.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

Initialed and dated copies of Applicant's IDS forms 1449, filed August 29, 2003 and September 2, 2003, are attached to the instant Office action.

One item of information in the IDS form 1449 filed September 2, 2003 fails to comply with all the requirements of 37 CFR 1.97 and 37 CFR 1.98; this item was not considered. Each publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, date, and place of publication.

Specification

The disclosure is objected to because of the following informalities: The specification fails to comply with 37 CFR 1.821(d), in that reference is not made to all sequences recited in the text by use of a sequence identifier preceded by "SEQ ID NO:". For example, see page 16. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 15, and claim 16 dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 15 is indefinite in the recitation of "D-like protein". It is unclear in what way the encoded protein is "like" D, as one protein may be like another in more than one way, such as structure(s), function(s), localization, pathway(s), etc., and the nature of the likeness of the encoded protein to a D protein is not disclosed in the specification or evident from the limitations recited in the claim. It is also unclear in what a D protein is, as "D protein" is not defined in the specification.

Claim Rejections - 35 USC § 101 and 35 USC § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 15 and 16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to a nucleotide sequence which encodes the plant D-like protein designated BRO4 as depicted in SEQ ID NO: 8, including the nucleotide sequence depicted in SEQ ID NO: 7.

The specification discloses that SEQ ID NO:7 is a partial cDNA sequence 626 nucleotides in length that encodes a 209 amino acid polypeptide of SEQ ID NO:8, and that SEQ ID NO:7 was obtained from an *Arabidopsis* library using a yeast two-hybrid system designed to screen for sequences that encode proteins that interact with the *Arabidopsis* D-type cyclin D1 (pages 25-27; sequence listing). The specification also discloses that SEQ ID NO:8 comprises a region of approximately 22 amino acids that is substantially homologous to the mammalian cyclin-dependent kinase binding domain consensus sequence. (page 27), but the specification does not disclose whether SEQ ID NO:7 encodes a protein having a specific function or activity. The specification further discloses that sequences encoding the protein designated BRO4 are useful for producing transgenic plant cells or plants having an increased growth rate and/or yield as a consequence of the expressed BRO4 protein binding and inactivating a plant D-like cyclin/cyclin dependent kinase complex (pages 4-5), but the specification does not disclose how to use SEQ ID NO:7 to achieve such an effect.

The claimed invention is not supported by a well established utility because the prior art does not teach a use for a nucleotide sequence of SEQ ID NO:7 or which encodes SEQ ID NO: 8.

The claimed invention is not supported by a specific and substantial asserted utility because no specific and substantial utility has been established for a nucleotide sequence of SEQ ID NO:7 or for a nucleotide sequence which encodes SEQ ID NO: 8.

The disclosure that that SEQ ID NO:7 encodes a polypeptide that interacts with the *Arabidopsis* D-type cyclin D1 does not establish a specific and substantial utility for a nucleotide sequence of SEQ ID NO:7 or for a nucleotide sequence which encodes SEQ ID NO: 8 because

the detection of a protein-protein interaction in a yeast two hybrid system is not necessarily indicative of a real world use for the specific coding sequence identified.

See, for example, Luban J. et al. (The yeast two-hybrid system for studying protein-protein interactions. Curr Opin Biotechnol. 1995 Feb;6(1):59-64. Review), who teach that proof of a direct interaction between proteins in a specific biochemical assay is the preferred approach to distinguishing between true and false positive interactions detected using the yeast two hybrid system, and that subsequent to the identification of a specific protein-protein interaction in a yeast two hybrid system, one must demonstrate its functional significance (page 62 column 1).

See also, for example, Caponigro G. et al. (Functional analysis of expressed peptides that bind yeast STE proteins. J Biotechnol. 2003 Aug 15;103(3):213-25), who used the yeast two-hybrid technique to identify and study peptide binders for three yeast proteins involved in pheromone response and found that only a subset of peptide binders was shown to inhibit pheromone response in cells using two different functional assays (abstract; page 218 Table 3; page 219 Table 4). Caponigro G. et al. also utilized a variant of the yeast two-hybrid method to examine relative binding affinities based on competitive interactions in yeast, and reported that their results suggest that binding affinity and inhibitory potency of peptides do not correlate perfectly, and that peptide-protein interactions can be complex and unpredictable (abstract; page 219 column 2 through page 221 column 2). Caponigro G. et al. concluded that taken together their results suggest that while peptides are useful as in vivo inhibitors of protein function, caution must be exercised when choosing peptides for further studies and when inferring affinities from expression phenotypes (abstract; page 224 column 1).

The disclosure that that SEQ ID NO:8 comprises a region of approximately 22 amino acids that is substantially homologous to the mammalian cyclin-dependent kinase binding domain consensus sequence does not establish a specific and substantial utility for a nucleotide sequence of SEQ ID NO:7 or for a nucleotide sequence which encodes SEQ ID NO: 8 because the function of a protein cannot reliably be predicted on the basis of its structure or its homology to other known proteins.

See, for example, Whisstock J.C. et al. (Prediction of protein function from protein sequence and structure. Q Rev Biophys. 2003 Aug;36(3):307-40. Review), who teach

> "... prediction of protein function from sequence and structure is a difficult problem, because homologous proteins often have different functions. Many methods of function prediction rely on identifying similarity in sequence and/or structure between a protein of unknown function and one or more well-understood proteins. Alternative methods include inferring conservation patterns in members of a functionally uncharacterized family for which many sequences and structures are known. However, these inferences are tenuous. Such methods provide reasonable guesses at function, but are far from foolproof." (Abstract)

Whisstock J.C. et al. also teach at page 309 that while the observation that similar sequences determine similar structures gives us general confidence in homology modeling, much less reliable is the widely held assumption that proteins with very similar sequences should by virtue of their very similar structures have similar functions. Whisstock J.C. et al. further teach at page 309 that to reason from sequence and structure to function is to step on much shakier ground, that while many families of proteins contain homologues with the same function, the assumption that homologues share function is less and less safe as the sequences progressively diverge, and that even closely related proteins can change function through divergence to a related function or by recruitment for as very different function in such cases the assignment of

function on the basis of homology in the absence of direct experimental evidence will give the wrong answer.

Whisstock J.C. et al. additionally teach at page 310 that a protein need not even change sequence to change function, as numerous proteins exhibit multiple functions in different cellular environments such that even if detailed in vitro studies on isolated proteins do identity a function we cannot be sure we know the molecules full repertoire of biological activities, and that nonhomologous proteins may conversely have similar functions.

Whisstock J.C. et al. further teach that while general hints based on protein sequence, structure, genomics and interaction patterns may be useful in guiding experimental investigations of protein function,

> "inferring protein function from knowledge of the function of a close homologue is like solving the clue of an American crossword puzzle. Finding the word that satisfies the definition may be difficult but the task in principle is straightforward. Working out the function of a protein from its sequence and structure is like solving the clue of a British crossword puzzle. It is by no means obvious which features of the definition are providing the real clues, as opposed to misleading ones. Also, for both types of puzzle and for the suggestion of a protein function, even if your answer appears to fit it may be wrong." (pages 311-312).

The disclosure that that sequences encoding the protein designated BRO4 are useful for producing transgenic plant cells or plants having an increased growth rate and/or yield as a consequence of the expressed BRO4 protein binding and inactivating a plant D-like cyclin/cyclin dependent kinase complex does not establish a specific and substantial utility for a nucleotide sequence of SEQ ID NO:7 or for a nucleotide sequence which encodes SEQ ID NO: 8 because the effect of expressing only part of a full-length polypeptide in transgenic plants varies depending on the fragment expressed.

See, for example, Zhou Y. et al. (The plant cyclin-dependent kinase inhibitor ICK1 has distinct functional domains for in vivo kinase inhibition, protein instability and nuclear localization. Plant J. 2003 Aug;35(4):476-89), who teach that expression of an N-terminal truncation of the *Arabidopsis* cyclin-dependent kinase inhibitor ICK1 increases ICK1 effects on transgenic plants, whereas expression of a C-terminal truncation of ICK1 greatly reduces or abolishes ICK1 effects on transgenic plants, as compared to control plants expressing the full-length ICK1 protein (page 476 Abstract; page 479 Figure 2; page 480 Table 1).

Claims 15 and 16 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins
Primary Examiner
Art Unit 1638

CC

Cynthia Collins
11/29/05